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ABSTRACT

The effects of obstetrical medication on neonatal behavior were studied using a sample of 64 Israeli infants from medicated and non-medicated mothers. Most medicated mothers received a base dose of 75 mg. of Meperidine plus a base dose of 25 mg. of Phenargan. Other drugs used included Demerol, Valium, Butalgin, Pitocin, Pantopon, Trilene, Naline, and Torecon. Few significant behavioral differences (as measured by the Brazelton Neonatal Behavioral Assessment Scale) were detected in the first month of life, and at 3 months of age there was no difference in performance on the motor and mental scales of the Bayley Scales of Infant Development. Comparative analyses using samples of American and Uruguayan infants and additional data from other studies of American newborns led to the conclusion that light levels of obstetrical medication do not appear to have significant effects on neonatal behavior. It is noted, however, that this conclusion may well be qualified by some initial population differences, by the measurement commonly used in the studies reviewed, and possibly by critical cut-off points dividing the levels of medication that will and will not affect neonatal behavior. It is recommended that, until more is known, mothers should use as little obstetrical medication as possible. A number of tables are included. (Author/MS)

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ABSTRACT

The effects of obstetrical medication on neonatal behavior were studied using a sample of Israeli infants from medicated and non-medicated mothers. Few significant behavioral differences were detected in the first month of life and there was no difference in Bayley Infant Scale Performance at three months of age. Comparative analyses using samples of American and Uruguayan infants and additional data from other studies of American newborns led to the conclusion that light levels of obstetrical medication do not appear to have significant effects on neonatal behavior. However, this may well be qualified by some initial population differences, by the measurements commonly used in the studies reviewed, and possibly by critical cut-off points dividing the levels of medication that will and will not affect neonatal behavior.

THE EFFECTS OF OBSTETRICAL MEDICATION ON THE
BEHAVIOR OF ISRAELI NEWBORN INFANTS AND SOME
COMPARISONS WITH OTHER POPULATIONS

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With the development of more refined and reliable measures of a wide range of neonatal behavior (Brazelton, 1973; Horowitz & Brazelton, 1973) it has become possible to make better assessments of the effects of obstetrical medication on the behavior of newborn infants. Almost all of the recent research that has been reported has been done on samples of infants born in the United States (Aleksandrowicz & Aleksandrowicz, 1974; Bowes, Brackbill, Conway & Steinschneider, 1970; Brackbill, Kane, Manniello, & Abrahamson, 1974; Standley, Soule, Copans, and Duchowny, 1974). In aggregate, the results implicate obstetrical medication as an agent in depressing orienting behavior in newborns, increasing irritability, and interfering with habituation to stimulation. Correlations with amount of dosage, particular drugs (e.g. meperidine) and drug combinations have been reported. Behavioral effects long past the time it is expected the drugs to have ceased active physiological functioning have also been suggested (Aleksandrowicz, 1974; Aleksandrowicz & Aleksandrowicz, 1974; Bowes, et al., 1970.)

However, several problems arise in interpreting the data summarized above and in using the results to aid obstetricians and their patients in making a choice for or against elective medication or in choosing specific medicants and dosage levels. Because obstetrical medication is routinely used in most American hospitals, finding samples of infants whose mothers have had no medication is difficult. These samples are necessarily small and in many ways select. Positive results showing drug effects are sometimes achieved only when the data are subjected to very sophisticated statistical procedures. In some cases one can question whether the sophistication of the statistical analyses might not be disproportionate to the grossness of the behavioral measures upon which the analyses are done. Finally, the absolute magnitude of significant differences in behavioral responses is sometimes so small as to raise questions concerning whether those differences have any

subsequent functional effects.

In contrast to standard obstetrical practice in American hospitals, medication is not necessarily used during labor and delivery in Israeli hospitals. At Kaplan Hospital, in Rehovot, Israel at the time the present study was conducted, obstetrical medication was administered to approximately 50% of the mothers delivering the infants. Medication was administered most systematically in births with complications where an obstetrician was in attendance. For routine births, attended by a licensed mid-wife, medication was not regularly administered, but was given relatively unsystematically, depending upon mid-wife preference, how crowded the labor room was, and mother request. Under these circumstances it was possible to arrange to test a relatively good-sized sample of infants whose births were uncomplicated where the mothers received no medication and to have a comparison sample of uncomplicated births where mothers did receive some medication. A study was planned that would replicate the design of the dissertation study by Aleksandrowicz (1973) and reported by Aleksandrowicz and Aleksandrowicz (1974) and by Horowitz, et al. (1973). This design called for testing infants daily on the first through fifth day of life, on the seventh and tenth days, and at one month of age using the Neonatal Behavioral Assessment Scale (Brazelton, 1973). However, the intervention of the Yom Kippur war forced a delay in the research and when it was resumed the neonatal assessments were reduced to Days 1 - 4 hospital, and a 1 - month assessment in the home. A 3-month Bayley Infant Scale examination was added.

The results of the study of the Israeli infants, as shown in the report that follows, were surprising on several dimensions. In order to better understand the alternative interpretations some comparisons were made between Israeli infants and two samples of American infants drawn from the dissertation data reported by Aleksandrowicz (1973). Data were also available on two samples of infants tested in Uruguay and some additional comparative analyses were possible. Thus, this report includes the description and results of the study involving Israeli infants and results from additional comparisons with American and Uruguayan infants. On the basis of the data included in this report we believe it is possible to draw more qualified and extensive conclusions regarding the possible effects of obstetrical medication on newborn behavior than has been feasible heretofore.

The major portion of this report is devoted to a description of the method and results of the Israeli study. This is followed by some comparative analyses of the Israeli and Kansas infants, a brief description of the study of the Uruguayan infants, and then a report of the results of the comparative analyses involving Israeli, Uruguayan, and American infants. An integrated discussion and interpretation of all the data concludes the article.

Method

Subjects

A total of 70 infants entered the Israeli study. For 64 infants we had at least five evaluations and these are the infants who constitute the sample on which

the major analyses were done. Of these 64 infants, 31 infants were born to mothers who received some medication during labor and delivery and 33 were born to mothers who received absolutely no medication. Table 1 describes the ages at which the tests were done and some of the population characteristics. All infants included

Insert Table 1 about here

in this study were full term, normal infants, vaginally delivered and without complications. All the infants were born to Jewish parents. Though subject intake was not controlled for parental background and origin, it turned out that approximately half the sample involved infants born to parents of Ashkenazic background and half to parents of Sephardic background. It further developed that approximately half of each of these ethnic origin groups was in the Drug and No Drug groups. All infants who were subjects in this study were conceived prior to the onset of the Yom Kippur war though the non-war period inutero ranged from two to seven months.

The different medications, the different combinations and dosages of medications and the frequency of their use with the Israeli Drug group is shown in Table 2. Twenty five of the 31 mothers of the infants in the Drug group received a base dose of 75 mg. of Meperidine plus a base dose of 25 mg. of Phenegran. For 10 mothers this was the only medication received. Eleven mothers received these base doses plus one other agent, while two received a third and one received a fourth additional agent. The remaining seven mothers did not receive any Meperidine or Phenegran and the agents given to them are listed under "Other" in Table 2. Neither local-regional anesthesia or general anesthesia was used in this sample.

Insert Table 2 about here

Procedure

The head mid-wife and her assistant selected all the infants seen in this study. However, these particular individuals were not necessarily the mid-wives in attendance at the birth of the infants selected. In order to regulate the rate of subject intake two infants whose mothers had received no medication and two infants whose mothers had received obstetrical medication who were born on the first two days of each week (Sunday and Monday) were chosen until the desired sample size had been reached with approximately an equal number of male and female infants in each group. This gave us about four new infants a week and functionally resulted in about one out of every forty infants born in Kaplan Hospital entering the study.

The head mid-wife and her assistant made a record of each infant selected, noting whether the infant was born to a mother who received medication or did not receive medication, and indicating the medications given, the dosage, and the approximate time of administration. An unmarked blue card was placed on the bassinet of each infant selected for the study and it was by this means that the examiners knew which infants were to be included in the research study. No identifying information concerning maternal medication was available until the entire study had been completed, thus enabling those doing the behavioral evaluations to remain completely "blind" as to maternal medication.

Four behavioral evaluations using the Neonatal Behavioral Assessment Scale (Brazelton, 1973) were done in the hospital - one each on Days 1 through 4 - and a fifth was done at the infant's home when the infant was approximately 1-month of age. At 3-months of age the infant was evaluated using the motor and mental scales of the Bayley Infant Scales of Development (Bayley, 1970). These evaluations were done in the out-patient clinic of Kaplan Hospital or in the infant's home if the clinic appointment was not kept.

Permission to test the infant was obtained from each mother by the senior author speaking to the mothers in limited Hebrew. Only one mother who was approached refused to allow her infant to participate in the study.

Four examiners participated in the collection of the data. To the extent possible, no infant was tested twice in a row by the same examiner. There was no discussion between examiners of individual infants tested for the entire duration of the study. All the examiners were trained to administer the Neonatal Behavioral Assessment Scale and met a criterion of .90 inter-rater reliability. The first and second authors of this article were two of the four examiners and were familiar with the design of the study. The other two examiners were not psychologists and neither was familiar with the design of the study or the literature relating to the present study.

The Neonatal Behavioral Assessment Scale yields scores ranging from 1 to 9 on each of 27 items and includes the following kinds of behaviors: habituation during sleep, visual and auditory responsiveness while alert, motoric behavior and such things as self-quieting ability, consolability when upset, peak of excitement, rapidity of buildup, and hand-to-mouth behavior. If an infant was awake at the beginning of the exam the first four items which required the infant to be asleep were omitted.

The Bayley Scales of Infant Development were administered by the same four examiners during the time infants were 3-months of age. Because two of the examiners were not Israeli and not fluent in Hebrew the Social Behavior Record part of the exam was omitted and only the Motor and Mental Scales were administered.

Results

The results from 22 of the 27 items on the Neonatal Behavioral Assessment Scale were subjected to analysis of variance. Four items were not analyzed because the number of infants for whom data was available on all five test days was too small for meaningful statistical analysis. These were the initial habituation items where it was necessary for the infant to be and remain asleep during the administration of the item. A fifth item (number of smiles) was not analyzed because the data were markedly skewed toward zero. Each of the remaining 22 items was subjected to an analysis of variance that included two between factors: Sex and Drug/No Drug Group; and one within factor: Tests (Age). The requirement that a score on an item was necessary for each of the five test days, and requirements of proportionality with unequal numbers in each cell resulted in the number of subjects contributing to the analysis of each item ranging from 40 to 55.

The names of the 22 items analyzed are listed in Table 6 (which shows the results of a subsequent analysis). Of the between factors, Sex was significant, overall, on only two items: Orientation to Inanimate Visual Stimuli (Female $X = 7.62$, Males $X = 7.17$, $F = 4.26$, $df\ 1, 40$, $p\ .05$) and Cuddliness (Female $X = 5.82$, Males $X = 5.13$, $F = 4.72$, $df\ 1, 40$, $p\ .05$). Though in each instance the females scored higher the magnitude of the difference was less than scale score point. On no item was the overall factor of Drug/No Drug group significant. Tests was a significant factor (at .05 or less) on 20 of the 22 items with the typical trend one of increasing from Day 1 to 1-month. Only on Orientation to an Animate Auditory Stimulus and on Rapidity of Build-up was Tests not an overall significant factor. On seven items the Tests trend was not a general increase over age. The trends on these items are summarized in Table 3.

Insert Table 3 about here

On only four items was there a significant interaction effect. On item 16 (Consolability) there was a significant Test by Sex interaction ($F = 3.47$, $df\ 4, 192$, $p\ .01$) in which females tended to show a faster decrease in consolability over the first four days than males but scored higher in consolability at 1-month.¹ The other three significant interactions were Drug Group by Test interactions. These occurred on item 9: Orienting to Animate Visual and Auditory Stimuli ($F = 2.38$, $df\ 4, 160$, $p = .054$); item 15 Defensive Movement ($F = 2.93$, $df\ 4, 168$, $p\ .05$); and item 24: Lability of State ($F = 3.86$, $df\ 4, 184$, $p = .005$). The data for item 15 are shown in Figure 2, and the data for item 24 are shown in Figure 4. On item 9 the mean scores for the Drug and no Drug group were very similar. The means all range between 7.25 and 8.14 over the first four days. The source of the interaction is the divergence at 1-month of age with the Drug

infants scoring higher (e.e. more responsive) than the No Drug infants. However, the magnitude of the difference is less than 1- scale score point ($X = 8.01$ vs $X = 7.85$). On item 15 (Defensive Movements), a higher score means more activity and more directed activity in relation to a cloth held over the infant's face. Over the first two days the Drug group infants are only slightly lower than the No Drug infants. But on Days 3 the Drug infants had a mean score of 5.0 while the No Drug infants had a mean score of 6.11. By Day 4 the magnitude of the differences increased ($X = 5.52$ vs $X = 6.78$). At 1- month of age, however the Drug infants had only a slightly higher score than the No Drug infants ($X = 6.7$ vs $X = 6.3$). On item 24 (Lability of State) a higher score indicates more state changes pro-rated against the length of the examination. On Days 1 and 2 the Drug Group infants showed significantly less state lability than the No Drug infants (Day 1: $X = 4.70$ vs $X = 5.70$; Day 2: $X = 5.80$ vs $X = 6.56$). By Day 3 the Drug group was slightly more labile ($X = 6.41$ vs $X = 6.38$) and this maintained on Day 4 ($X = 6.64$ vs $X = 6.07$). At 1-month of age the No Drug group showed significantly less state lability than the Drug group and the magnitude of the difference was among the larger ones on any of the items ($X = 3.40$ vs $X = 5.22$).

To summarize the results of the Israeli infants born to mothers who did and did not receive medication it can be said that while there were many differences attributed to sex, and there were a few differences that could be attributed to the factor of medication as reflected in the behaviors measured by the Neonatal Behavior Assessment Scale. On the 22 items included in the analyses there were none which showed an overall drug effect. Three items showed a significant interaction of medication and age. On the one orientation item where this was true the magnitude of differences was consistently less than one scale score point. Only on the item measuring lability of state did the magnitude of differences between the Drug and No Drug group infants exceed more than 1.5 scale score points. One could therefore conclude that medication effects were small but significant on one measure of orientation, were slightly larger on the measure of defensive movement, and were largest on the measure of state lability. Perhaps the most impressive result with regard to the medications factor is the finding that at 1-month of age Drug infants showed significantly more lability of state than No Drug infants and the magnitude of this difference (1.73 scale score points) is the largest one of all of the significant differences involving medication. On the other hand, considering the number of comparisons made on these data, this significant difference could have occurred by chance.

On 49 of the infants we had results of a 3-month Bayley test: 24 were done on infants in the No Drug group and 25 were done on infants in the Drug group. The data from the mental and motor scales were each analyzed using a 2 X 2 factorial ANOVA that included Drug Group and Sex as the two between factors. There were no significant differences revealed in these analyses. The overall mean for the Israeli infants on the Mental Scale was 111.9 and the mean on the Motor Scale was 105.79.

Comparisons Between Israeli, Kansas, and Uruguyan Infants

Two analyses involving a comparison of the Israeli infants with infants from other samples were carried out. The first analysis compared Israeli infants with two groups of infants tested in Kansas and the second analysis compared the Israeli infants and the Kansas infants with two groups of infants tested in Montevideo, Uruguay.

Subjects

The same Israeli infants were included in this analysis as contributed to the groups reported in the above analyses. Two groups of Kansas infants were extracted from the data reported in a dissertation by Aleksandrowicz (1973). One was a group of 8 infants born in Topeka, Kansas whose mothers had received general anesthetic. The second group consisted of 26 infants, also born in Topeka, whose mothers had received moderate to heavy medication.² The sample characteristics are shown in Table 4. In order to describe the drugs given the 26 mothers who comprised the moderate to heavy medication group one would need 24 separate

Insert Table 4 about here

descriptor groups as only three mothers received the same combination of drugs in the same dosages. A description of the medication used in the Kansas sample is given in Table 5. In seven of the eight instances where general anesthetic was used the mothers had received 50 or 100 mg. of Demerol as premedication and anywhere from one to four other medications; in one instance Morphine had been given.

Insert Table 5 about here

At the time that the Kansas data were collected general anesthesia was being used with some frequency in routine normal deliveries in the hospital where the study was being done.

Procedure

The infants in the Kansas sample were part of a dissertation study reported by Aleksandrowicz (1973) in which infants were tested a total of eight times using the Neonatal Behavioral Assessment Scale (Day 1-4, 7, 10, and 1-month).

In all ways the procedure was similar to that followed in the Israeli study except that deliveries were made by obstetricians rather than mid-wives. Seven trained testers helped collect the data (two of them were the second and third authors on this article) and testers remained blind as to the drug history of the infant's mother.

The Days 1-4 data and the 1-month data were extracted for the two samples and they were included in an overall ANOVA for each of the 22 items from the neonatal Behavioral Assessment Scale that compared the behavior of the two Kansas infant groups with the two Israeli groups. The ANOVA included one between factor of Groups and one within factor of Test Days. There were four groups: Kansas Moderate-Heavy Drug Group, Kansas General Anesthetic, Israeli Drug, and Israeli No-Drug. Sex was not included in this analysis because of statistical considerations and because of the relative infrequency of sex as a significant factor in a number of studies using the Neonatal Behavioral Assessment Scale (Horowitz & Brazelton, 1973; Osofsky & Danzger, 1974).

Results

The group means and results of the analysis are shown in Table 6. As can be seen, on 18 of the 22 items the overall factor of groups was significant; on

Insert Table 6 about here

15 of the 22 items Test Days yielded significant results. On eight items the Groups by Test Days interaction was significant. Figures 1 to 4 illustrate the results from 12 items and include all the items on which there were significant Group X Test interactions.

Insert Figure 1 about here

Insert Figure 2 about here

Insert Figure 3 about here

Insert Figure 4 about here

The pattern of results shown in Table 6 and in Figures 1-4 are further revealed in the multiple comparison test results. Using the Tukey B test for multiple comparisons (Wike, 1971) it was found that on all 18 items where Groups was a significant factor the Kansas Moderate-Heavy Drug group mean scores were significantly different from both the Israeli groups. The direction of the differences was uniform: on orientation and motor items the Kansas infants scored lower than the Israeli infants though the magnitude of the differences is largest on the orientation items (See means in Table 6). On items 5 through 14, 16, 17, 20, 25 and 26 the Kansas General Anesthetic group is also significantly different from the two Israeli groups with the direction and the relative magnitude of differences similar to the Kansas Moderate-Heavy Drug group and Israeli group comparisons. On items 15 and 18 the Kansas General Anesthetic group is only different from the Israeli No Drug group. The two Kansas groups differ significantly from each other on eight items (5, 6, 7, 9, 10, 17, 23, and 24) while the two Israeli groups (as reported above) did not show an overall significant difference as a function of Drug group on any item.

On seven items there was a significant interaction between test days and groups. On item 13 (Pull-to-Sit) the source of this interaction can be seen on Figure 2: At 1-month of age the direction of the trend for the Israeli infants is upward (increased head control on Pull-to-Sit) while for the Kansas infants it is either relatively the same or downward with the relative magnitude of difference between the Kansas and Israeli infants at 1-month approaching almost 4- scale score points.³ On item 15 (Defensive Movement) a partially similar pattern of differences emerges though the overall magnitude of differences is much less. On item 19 (Irritability) the source of the interaction is in the significantly lowered irritability on Day 1 for the Kansas General Anesthetic group and the significantly increased irritability on Days 2, 3, and 4 for this same group. Another contributing element to the interaction is the significantly lower irritability of the Israeli No Drug infants at 1-month of age. On item 23 (Lability of Skin Color) the source of the significant interaction is in the decreased lability of the Israeli No Drug infants at 1-month of age. On item 24 (Lability of State) the only group that does not show significant changes over test days is the Kansas Moderate-Heavy Drug group while on item 26 (Hand to Mouth) neither Kansas group shows significant changes over test days but the two Israeli groups do.

Kansas, Israeli, and Uruguayan Infants

Subjects and Procedure

A sample of 80 infants was tested at 3- days of age in two different

hospitals in Montevideo, Uruguay by three trained testers. One of these testers was the second author of this article, one was a head nurse at one of the hospitals and the third was an M.D. pediatric neurologist. Fifty-one of the infants were born to mothers who had received no medication while 29 were born to mothers who had received some medication. In the medicated mothers 23 different descriptor groups would be needed to describe the sample because only two mothers received the same medicating agents in the same dosages. However, 14 of the mothers received one dose of Meperidine. For two that was the entire dosage; six received only one other medicant with the Meperidine, and six received two other medicants. The remainder of the 15 subjects included a variety of drug administrations involving Syntocinon, Lofan, Sertal Compuesta, Valium, Thorazine, Phenegan, Coramine, and Urtocaina. The dosages as taken from the hospital records were listed in ampules. Subsequent attempts, once the American tester returned to the United States, to find out the mg. equivalent of each of the ampules used has been unsuccessful but from the drugs used and their typical dosages it would appear that the Uruguayan Drug group infants would be classified as light to moderate levels of medication and comparable, therefore, to the Israeli Drug group.

The No Drug infants tended to be born in the Social Security hospital, while the Drug group infants were born mostly in the British hospital and were generally of higher socio-economic class than the No Drug infants. The mean birth weight of the No Drug male infants was 3.42 kg, for the No Drug female infants it was 3.30 kg., for the Drug male infants it was 3.37 kg., and for the Drug females it was 3.27 kg.

The Kansas and Israeli data used in this analysis were from the infants described previously. In each case the 3-day test performance was used for purposes of comparison with the Uruguayan infants. The 3-day test scores on each item were subjected to a simple randomized ANOVA comparing the mean performance of six groups of infants at 3-days of age. The six groups were: Group 1 - Kansas Moderate-Heavy Drug group; Group 2 - Kansas General Anesthesia; Group 3 Israeli Drug; Group 4 - Israeli No Drug; Group 5 - Uruguayan Drug; and Group 6 - Uruguayan No Drug. Because the data from only one day was analyzed it was possible to include in this analysis the data from the first four habituation items measured on the Neonatal Behavioral Assessment Scale. The n for these items was, however, smaller than the overall n for the remainder of the items because of the frequency with which infants awoke during the administration of these items.

Table 7 shows the means for each of the groups for each of the items and whether or not the F value yielded in the ANOVA was significant. On none of the

Insert Table 7 about here

habituation items (1 thru 4) were there any significant differences among the groups. On 15 of the remaining 22 items the F value was significant at or beyond the 5% level. The results of the Tukey B test comparisons between groups on those items where the ANOVA F value was significant are shown in Table 8. The pattern that emerges from that display shows the Kansas groups differing from the Israeli

Insert Table 8 about here

and Uruguayan groups much more frequently than the Israeli and Uruguayan groups differ from each other. Also the two Kansas groups differ from each other more frequently than the two Israeli groups or the two Uruguayan groups differ from each other. An examination of the means in Table 7 reveals that the magnitude of differences is largest between the Kansas infants and the other groups. This is particularly true on the orientation items (items 5 - 10), on Consolability (item 16), on Lability of State (item 24), and on Self Quieting Behavior (item 25). The lack of significance on the items of Peak of Excitement (item 17) Irritability (item 19), Activity Level (item 20), Tremulousness (item 21), and Startle (item 22) suggests that these factors cannot account for the other observed differences. In relation to the Drug and No Drug comparisons the Israeli and Uruguayan infants at 3 days of age (groups 3 vs 4 and groups 5 vs 6) do not show many differences. In comparing the Israeli Drug group and the Uruguayan Drug group (3 vs 5) there are differences on three of the orientation items, on Consolability, Lability of State and Hand-Mouth facility. A comparison of the two non-Drug groups (4 vs 6) revealed similar differences. In addition there were differences on General Tonus (item 11), Rapidity of Build-up (item 18), and Self-Quieting Behavior (item 25).

Discussion

What can one say about the effects of obstetrical medication on the behavior of newborn infants? There are two comparisons in the data reported in this article that involve larger groups of No Drug infants than has heretofore been available. We found few significant differences between the Drug and No Drug Israeli infants. Where there were differences the magnitude of those differences was small. The possible exception to this was on Defensive Movements where on Days 3 and 4 the Drug infants showed less active response to a cloth on the face; the other possible exception and perhaps an important one was the lowered state lability on Days 1 and 2 for the Drug infants but significantly higher lability at one month of age.

The No Drug and Drug group comparisons of the Uruguayan infants yield results comparable to the findings with the Israeli infants. Despite differences in socio-economic status between the two Uruguayan groups few significant differences were found. These findings replicated most of the Israeli findings despite the fact that on the Uruguayan infants we had only one assessment and on the Israeli infants

we had five neonatal assessments.

The comparison of the Kansas infants to the Israeli and Uruguayan infants is complicated by the fact that the drug factors are different. The Kansas infants had mothers who were much more heavily-medicated than the mothers in either the Israeli or the Uruguayan drug groups. Whether this accounts for the generally depressed orienting behavior and poorer state control among the Kansas infants is difficult to determine. A fairly good sized No Drug group of Kansas infants could help us evaluate these differences but unfortunately such data are not available. However, there are several small samples of American No Drug infants that have been included in various studies. Aleksandrowicz (1973) had five such infants in her Kansas sample, Tronick, Wise, Als, Adamson, Scanlon and Brazelton (1975) had six in a Boston sample, and Standley, et al. (1974) had seven infants in a Washington D. C. area sample whose mothers had received no medication. The latter two groups of investigators kindly provided the mean scores on the items of the Neonatal Behavioral Assessment Scale for their No Drug infants and Standley also provided the means for a group of infants whose mothers had received only analgesic pre-medication at levels comparable to the Israeli and Uruguayan infants. These means are shown in Table 9. (The first four habituation items are excluded because data were not obtained on all the infants in the No Drug groups). Several interesting comparisons may be made from the data shown in Table 9 if they are compared to the

Insert Table 9 about here

means shown in Table 7, though one must be cautious because of the small numbers. If one takes the means of the orientation items (items 5 thru 10) and calculates a mean of these six items for each group the following results are obtained: Kansas No Drug, 5.4; Kansas Moderate-Heavy Drug, 4.9; Kansas General Anesthesia, 5.1; Israel No Drug, 6.8; Israel Moderate Drug, 6.8; Uruguay No Drug, 6.2; Uruguay Moderate Drug, 6.4; Boston No Drug, 6.5; Washington, No drug, 6.5; and Washington, Moderate Drug, 5.2. The Boston and Washington No Drug group means resemble the Israeli and Uruguayan groups on the absolute level of response on the orientation items; the Kansas infants are generally lower on these items; the Washington Moderate Drug group looks more like the Kansas infants. In the data published by Ososky and Danzger (1974), where the medication levels reported suggests that the sample is somewhat similar to the Kansas Moderate-Heavy Drug group, the overall mean of the Orientation items is 4.9. Similarly, Strauss, Lessen-Firestone, Starr & Ostrea (1975), in a Detroit sample with comparable medication, also reported data which yielded a mean of 4.8 on the orientation items. The No Drug group comparisons put the Kansas infants more than one scale score point lower than the Israeli infants and almost one scale point lower than the Boston and Washington infants.

One reason why one scale score point is being used as a metric in evaluating the magnitude of the differences is because examiner reliability on the Neonatal Behavioral Assessment Scale is defined as examiners scoring the same or one score different on each item. During training examiners who both score 5 on an item are considered reliable; if one examiner scores 5 and one scores 6 their scoring is also counted as reliable. Thus, statistically significant differences of less than one scale score point are questionable in terms of the meaning of the differences. Of the 15 within-population differences of the Kansas, Israeli and Uruguayan groups (i.e. Kansas v. Kansas, Israeli v. Israeli, etc.) that were statistically significant (Table 8) in only three instances was the magnitude more than one scale score point and these all involved the two Kansas Drug groups. In contrast, if one looks at the means displayed in Table 9 the magnitude of the differences for the two Washington samples exceeds one scale point on 11 items; comparing the Kansas No Drug means in Table 9 with the two Kansas Drug groups' means in Table 7 there are also 11 differences which exceed one scale score point. Because of the small size of the Kansas and Washington No Drug samples one must be cautious in drawing conclusions. But, it is the case that there are no differences between the Israeli No Drug and Drug groups or the Uruguayan No Drug and Drug groups where the magnitude of the differences exceeds one scale score point. Perhaps larger samples of Kansas and Washington No Drug infants would produce similar results.

Nevertheless, on the basis of the data reported in this article one must entertain several propositions. The first is that there are population differences with respect to the relative effect of obstetrical medication on neonatal behavior. Perhaps some populations have initially stronger response repertoires in certain dimensions; these response systems may be more resistant to the effects of obstetrical medication and this combines with other factors in affecting neonatal behavior. Yang, Zweig, Douthitt, & Federman (1976) have argued for a potentiating factor of maternal attitudes on drug effects. It is possible that genetic, biological, and attitudinal factors combine to determine the subsequent effect of obstetrical medications on neonatal behavior. Unfortunately, we have no attitudinal measure on the Israeli or Uruguayan infants. However, all the Israeli infants were born during wartime.

The second proposition is that there maybe a critical cut-off point with regard to neonatal behavior being affected by drugs. Before a certain point (and that point may differ for different populations as well as for different individuals) obstetrical medication will show few effects on neonatal behavior. Tronick, et al. (1975), found few differences in their entire sample of Boston infants, none of whose mothers had received heavy medication and they attributed their results to the relatively light levels of medication and to the very selective procedures they used in getting their sample. In neither the Uruguayan or Israeli studies were the infants as selected as those in the Boston study, yet the same results were obtained indicating few effects on infant behavior attributable to obstetrical medication. On the other hand in three American samples with

moderate to heavy obstetric medication (Kansas Moderate-Heavy Drug Group, Osofsky & Danzger's Philadelphia infants and Strauss, et al.'s Detroit infants) the means of the orientation items (4.7 to 4.9) were much lower than the means of these items in samples with either no medication or lighter medication.

The third proposition is really an important qualification. Common to all the studies reviewed and compared here is the Neonatal Behavioral Assessment Scale. The Scale uses the best behavior of the neonate as the basis for scoring. Perhaps a scoring technique that took into account more than the best behavior would produce some different results. In that case, both drug effects and population differences might well be magnified. Such a scoring procedure is presently under development by the senior author and his students.

One must conclude, on the basis of data presented here and using some of the comparisons with other studies, that light to moderate levels of obstetrical medication do not influence neonatal behavior. Yet, one must remain cautious and qualify such a conclusion by the nature of the populations studied, by the characteristics of the measuring instrument used, and by our lack of knowledge concerning exactly what magnitude of differences in behavior are functional in affecting subsequent development. Osofsky & Danzger (1974) have presented evidence to suggest that mother-infant interaction patterns are significantly affected by neonatal infant behavior characteristics. Until we know the critical magnitudes of differences in those characteristics and the influence of obstetrical medication on the size of the differences the best guidance we can offer in regard to the use of obstetrical medication from the standpoint of infant behavior is "use as little obstetrical medication as possible".

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Table 1

Characteristics of Israeli Infants

	Drug Group		No Drug Group	
	Males	Females	Males	Females
	15	19	17	14
Mean Hours Age At Test				
Tests 1	8.40	9.38	9.38	8.10
Tests 2	29.30	28.62	28.88	28.20
Tests 3	50.00	50.86	50.25	50.20
Tests 4	72.70	72.81	73.00	72.90
Mean Days Age at 5th Testing				
Mean				
Birthweight	3.22 kg	3.12 kg	3.52 kg	3.30 kg
Mean Birth Order Of Infant				
	1.67	1.54	2.33	2.33

Table 2

Distribution of Medication and Dosages in the Israeli Drug Group

Meperidine and Phenergan Group:	n
Meperidine (75mg) + Phenergan (25 mg) (Demerol)	10
Meperidine (75 mg) + Phenergan (25 mg) + either Valium (10 mg) or Butalgan or Pitocin (5cc) or Pantopon (20 mg) or Trilene	11
Meperidine (75 mg) + Phenergan (25 mg) + Pitocin (5cc) + Naline (5 or 10 mg)	2
Meperidine (75 mg) + Phenergan (25 mg) + Pitocin (5 mg) + Valium (10 mg) + Torecon (5 mg) + Pantopon (20 mg)	1
Other:	
Torecon (5 mg) + Butalgan (5cc) + Trilene gas	1
Pantopon (20 mg) + Torecon (5 mg) + Butalgan	1
Butalgan + Trilene	1
Pantopon (20 mg) + Torecon (5 mg)	1
Trilene only	1
Valium only	1
Butalgan only	1

Registered under various brand names: e.g. Pethidine and Demerol

Table 3

Direction of Some Significant Tests Trends
in Israeli Infants on Brazelton Test Items

Item	Description of Trend
16. Consolability	Decrease from Day 1 to Day 4, Increase from Day 4 to 1 month
19. Irritability	Increase from Day 1 to Day 3, Decrease from Day 4 to 1 month
21. Tremulousness	Increase Day 1 to Day 2, Decrease from Day 2 to 1 month
22. Startle	Decrease from Day 2 to 1 month
23. Skin Color Lability	Decrease from Day 2 to 1 month
24. Lability of State	Increase from Day 1 to Day 4, Decrease from Day 4 to 1 month
26. Self-Quieting	Decrease from Day 1 to Day 4, Decrease from Day 4 to 1 month

Table 4

Characteristics of Kansas Infants

Moderate to Heavy (N=26)

Mean Age in Hours

Day 1	16.48
Day 2	39.92
Day 3	64.96
Day 4	87.90
Day 5	28.34 (Days)

Moderate to Heavy (N=26)

Means For

Birth Wt.	Birth Order	Mother's Age
lbs. kg.		
7.41 3.36	1.69	26.5

General Anesthetic (N=8)

Mean Age in Hours

Day 1	15.56
Day 2	33.18
Day 3	58.12
Day 4	81.39
Day 5	29.00 (Days)

General Anesthetic (N=8)

Means For

Birth Wt.	Birth Order	Mother's Age
lbs. kg.		
8.02 3.63	2.00	26.3

Table 5

Medication Characteristics of Kansas Sample of Moderate to Heavy Drug Group

No. Different Agents Administered	Frequency in Sample
1	1
2	1
3	5
4	4
5	6
6	8
9	1

Specific Agents Used

I. Central Nervous System Depressants

A. Synthetic Narcotic Analgesics

1. Nisentil	8
2. Meperidine	8
3. Mepergan	12

B. Narcotic Analgesic

1. Morphine	3
-------------	---

C. Short-Acting Barbiturate

1. Seconal	5
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D. Tranquilizers

1. Valium	2
2. Atarax	1

II. Uterine Stimulants

1. Pitocin & Buccal Pitocin	14
2. Syntocinon	9
3. Quinine	2

Table 5 (contd.)

Medication Characteristics of Kansas Sample of Moderate to Heavy Drug Group

Specific Agents Used	Frequency in Sample
III. Anesthetics	
A. Nerve Block (Site)	
1. Pudendal	3
2. Saddle	9
B. Local	
1. Xylocaine	7
2. Pontocaine	3
C. Inhalants	
1. Nitrous Oxide	11
2. Penthrane	6

Table 6

Kansas and Israeli Data

Item No.	Scale	Anova Results		Group Means			
		Group	Test Days	Group 1 (Kansas Moderate- Heavy Drug)	Group 2 (Kansas General Anesthesia)	Group 3 (Israeli Drug)	Group 4 (Israeli No Drug)
5.	Inanimate Visual	S	S	4.7	4.1	7.3	7.4
6.	Inanimate Auditory	S	NS	4.7	3.8	6.7	6.8
7.	Animate Visual	S	S	5.6	4.9	7.2	7.4
8.	Animate Auditory	S	NS	5.5	5.3	6.9	6.8
9.	Animate Visual & Auditory	S*	NS	5.7	4.9	7.5	7.7
10.	Alertness	S	NS	4.2	3.7	6.4	6.6
11.	General Tonus	S	S	4.8	4.7	5.8	5.8
12.	Motor Maturity	S	S	4.0	3.9	5.4	5.7
13.	Pull-to-Sit	S*	S	4.2	4.2	5.9	6.1
14.	Cuddliness	S*	S	5.0	4.7	5.6	5.5
15.	Defensive Movement	NS*	S	5.6	5.3	5.6	6.1
16.	Consolability	S	NS	4.8	4.7	8.8	8.5
17.	Peak of Excitement	S	S	5.9	6.5	5.5	5.8
18.	Rapidity of Buildup	S	NS	4.6	4.4	3.9	3.8
19.	Irritability	NS*	S	4.1	4.2	3.7	3.7

Table 6 (Contd.)

Kansas and Israeli Data

Item No.	Scale	Anova Results		Group Means			
		Group	Test Days	Group 1 (Kansas Moderate- Heavy Drug)	Group 2 (Kansas General Anesthesia)	Group 3 (Israeli Drug)	Group 4 (Israeli No Drug)
20.	Activity	S	S	4.6	4.7	5.1	5.2
21.	Tremulousness	NS	S	3.7	3.5	3.7	3.9
22.	Startle	NS*	NS	3.1	3.4	2.8	2.8
23.	Lability of Skin Color	S*	S	4.7	5.5	5.4	5.4
24.	Lability of State	S*	S	4.6	5.3	5.7	5.8
25.	Self-quieting Activity	S	S	5.4	5.0	7.8	7.6
26.	Hand-Mouth Facility	S*	S	4.5	4.0	3.6	3.6

S - groups significant at $p = < .05$

S* - groups significant and interaction of groups and test days significant at $p = < .05$

NS - not significant

NS* - groups not significant but interaction with test days significant at $p = < .05$

Table 7

Kansas, Israel, and Uruguay Means on Day 3

Scale Item	F value	Group 1 (Kansas Moderate/ Heavy Drug)	Group 2 (Kansas General Anesthesia)	Group 3 (Israeli Drug)	Group 4 (Israeli No Drug)	Group 5 (Uruguay Drug)	Group 6 (Uruguay No Drug)
	N	26	8	34	31	51	29
1. Decrement to Light	NS	4.8	4.0	5.2	5.8	5.2	6.2
2. Decrement to Rattle	NS	5.9	5.3	5.6	6.5	6.2	6.7
3. Decrement to Bell	NS	5.3	5.9	5.7	6.7	6.1	6.9
4. Decrement to Pinprick	NS	4.4	4.8	4.3	5.0	4.8	4.9
5. Inanimate Visual	S	4.5	4.3	7.1	6.9	5.8	5.5
6. Inanimate Auditory	S	4.7	4.1	6.6	6.3	5.8	5.6
7. Animate Visual	S	5.2	5.5	7.2	7.1	6.7	6.4
8. Animate Auditory	S	5.3	5.8	6.7	6.6	6.6	6.7
9. Animate Visual & Auditory	S	5.6	5.6	7.5	7.3	7.2	7.1
10. Alertness	S	4.0	5.2	6.0	6.3	6.3	6.1
11. General Tonus	S	5.0	4.7	6.0	5.7	6.1	6.1
12. Motor Maturity	S	3.7	4.8	5.2	5.4	5.4	5.4
13. Pull-to-Sit	S	4.7	5.2	6.4	6.3	6.6	6.0
14. Cuddliness	NS	4.9	5.4	5.6	5.6	5.5	5.1

Table 7 (contd.)

Kansas, Israel, and Uruguay Means on Day 3

Scale Item	F value	Group 1 (Kansas Moderate/ Heavy drug)	Group 2 (Kansas General Anesthesia)	Group 3 (Israeli Drug)	Group 4 (Israeli No Drug)	Group 5 (Uruguay Drug)	Group 6 (Uruguay No Drug)
15. Defensive Movement	NS*	6.0	5.8	5.5	6.2	6.8	5.7
16. Consolability	S	4.0	4.4	8.1	8.2	7.6	7.4
17. Peak of Excitement	NS	6.2	5.6	5.9	6.0	6.2	6.2
18. Rapidity of Buildup	S	4.1	4.9	3.8	4.3	4.2	4.9
19. Irritability	NS	3.8	5.2	4.2	4.3	4.2	4.7
20. Activity	NS	4.6	5.1	5.3	5.1	5.3	5.4
21. Tremulousness	NS	3.8	3.4	4.4	4.2	4.0	4.2
22. Startle	NS	3.2	3.4	3.0	3.3	3.4	2.9
23. Lability of Skin Color	S	4.0	5.2	5.4	5.8	5.9	NA
24. Lability of State	S	4.2	5.3	6.5	6.1	7.0	5.7
25. Self-quieting Activity	S	4.5	4.3	7.1	7.6	7.0	6.6
26. Hand-mouth Facility	S	4.1	5.2	4.1	4.0	6.4	5.7

S - significant

NS - not significant

* - approached significance at .052

NA - not available because of generally dark skin color

Table 8

Results of Tukey B Comparisons of Differences Between
Kansas, Israeli, and Uruguayan Infants at 3 Days of Age

Item Name	Comparison Groups														
	1-6	1-5	1-4	1-3	1-2	2-6	2-5	2-4	2-3	3-6	3-5	3-4	4-6	4-5	5-6
5. Inanimate Visual	x	x	x	x		x	x	x	x	x	x		x	x	
6. Inanimate Auditory	x	x	x	x	x	x	x	x	x	x	x		x	x	
7. Animate Visual	x	x	x	x		x	x	x	x	x	x		x		
8. Animate Auditory	x	x	x	x	x	x	x	x	x						
9. Animate Visual & Auditory	x	x	x	x		x	x	x	x	xx					
10. Alertness	x	x	x	x	x	x	x	x	x	x					
11. General Tonus	x	x	x	x	x	x	x	x	x			x	x	x	
12. Motor Maturity	x	x	x	x	x	x	x	x	x						
13. Pull-to-Sity	x	x	x	x	x	x	x	x	x						x
14. Consolability	x	x	x	x		x	x	x	x	x	xx		x	xx	
18. Rapidity of Buildup	x				x		x	x	x	x			x		x
23. Lability of Skin Color	NA	x	x	x	x	NA	x			NA			NA	x	NA
24. Lability of State	x	x	x	x	x	x	x	x			x	x			
25. Self-quieting Activity	x	x	x	x		x	x	x	x				x	xx	
26. Hand-Mouth Facility	x	x			x		x	x	x	x	x		x	x	x

x = significant at less than .01

xx = significant at less than .05

NA = Not available

Table 9

Means from Kansas, Boston, and Washington, D. C.

Samples - 3 Days of Age

	Kansas No Drug ^a N=5	Boston No Drug N=6	Wash., D.C. No Drug N=7	Wash., D.C. Analgesic Only N=38
5. Inanimate Visual	5.2	6.0	6.1	4.6
6. Inanimate Auditory	4.2	6.1	6.4	5.0
7. Animate Visual	6.0	6.6	6.8	5.6
8. Animate Auditory	4.8	6.5	6.5	5.7
9. Animate Visual & Auditory	6.4	6.8	7.2	6.3
10. Alertness	6.2	7.1	6.1	4.3
11. General Tonus	5.4	5.5	6.0	6.0
12. Motor Maturity	4.6	5.3	6.2	4.2
13. Pull-to-Sit	4.4	6.1	5.4	5.1
14. Cuddliness	5.0	6.6	5.0	4.5
15. Defensive Movement	7.8	6.9	5.8	5.2
16. Consolability	5.8	6.6	5.2	5.4
17. Peak of Excitement	6.8	5.8	5.7	6.2
18. Rapidity of Buildup	4.4	4.3	2.6	4.3
19. Irritability	4.4	3.6	2.7	3.9
20. Activity	5.2	4.8	4.7	5.2
21. Tremulousness	5.8	3.6	2.5	5.3
22. Startle	3.2	3.3	2.5	5.2
23. Lability of Skin Color	3.8	4.1	NA	NA
24. Lability of State	3.8	3.1	3.2	3.8
25. Self-quieting Activity	5.8	5.5	4.0	5.4
26. Hand-Mouth Facility	5.6	5.8	6.7	6.4

^a from Aleksandrowicz, 1973-corrected data
NA = Not available

Figure Captions

Figure 1. Neonatal Behavioral Assessment Scores for Two Groups of Israeli and Kansas Infants on Orientation to Inanimate Visual Stimuli, Orientation to Animate Visual Stimuli, General Tonus, and Motor Maturity.

Figure 2. Neonatal Behavioral Assessment Scores for Two Groups of Israeli and Kansas infants on Pull-To-Sit, Cuddliness, Defensive Movements, and Peak of Excitement.

Figure 3. Neonatal Behavioral Assessment Scores for Two Groups of Israeli and Kansas Infants on Irritability, Activity, Tremulousness, and Startles.

Figure 4. Neonatal Behavioral Assessment Scores for Two Groups of Israeli and Kansas infants on Lability of Skin Color, Lability of States, Self-Quiescent Activity, and Hand-to-Mouth Facility.

Footnotes

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1. The means for the males ranged from 8.07 to 9.01 while the means for the females ranged from 7.67 to 9.45. However, on about 48% of the examinations the infants did not cry or they self-quieted everytime they cried so that there was no opportunity to console the infant and therefore no way to score the infant in terms of how much was required to console the infant. For only three infants did we have a consolability score on all five examinations. Rather than discard this item from our analysis a score of 10 was given if the infant did not require consoling during the exam. The overall mean on this item for the whole sample was 8.65 using 10 for instances when the infant never required consoling. The overall mean for just those examinations when consoling was scored was 7.30. This is a relatively high mean compared to other samples and indicates that when the infants in this sample required consoling they tended to be consoled without a great deal of effort of the examiner.
2. There were 16 additional infants in Aleksandrowicz' sample: 5 infants had mothers who received no medication. Because of the small n this group was not included in the present analysis. There were eleven subjects where the amount of complete test data was insufficient to be included in this analysis. Because of transcribing errors found in the computer print out of the Aleksandrowicz thesis data the data used in this analysis were taken directly from the original score sheets and checked until the transcribing was found to be error free.
3. Full details of the results of all the statistical results of all the multiple comparisons are available, upon request, from the senior author.
4. Full details of the results of all the statistical results of all the multiple comparisons are available, upon request, from the senior author.

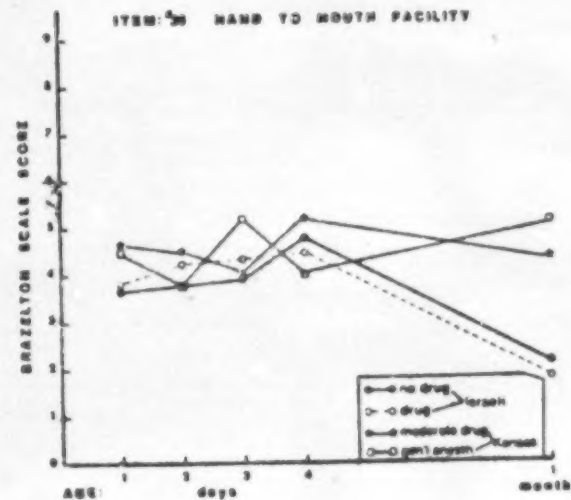
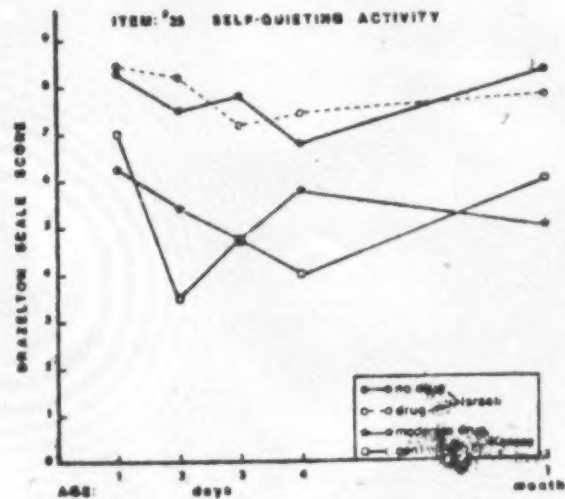
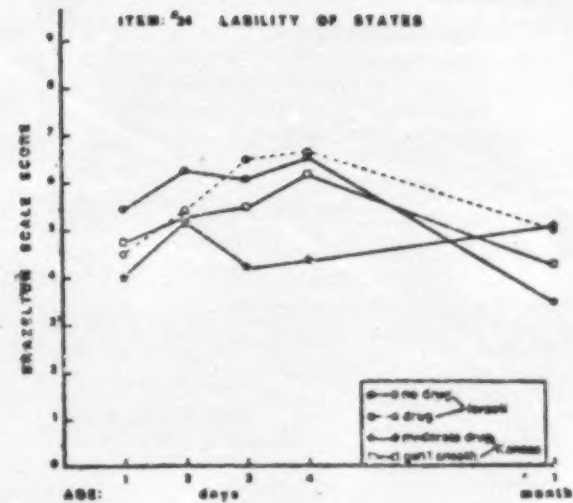
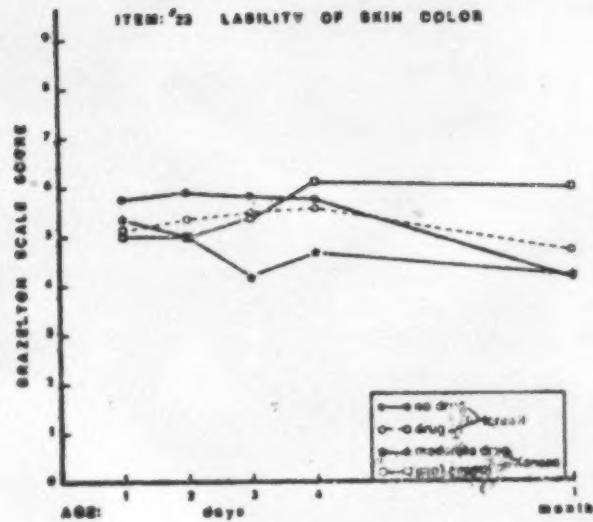
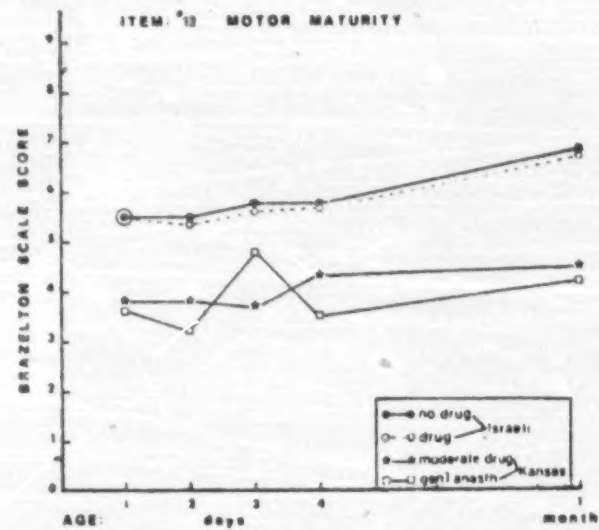
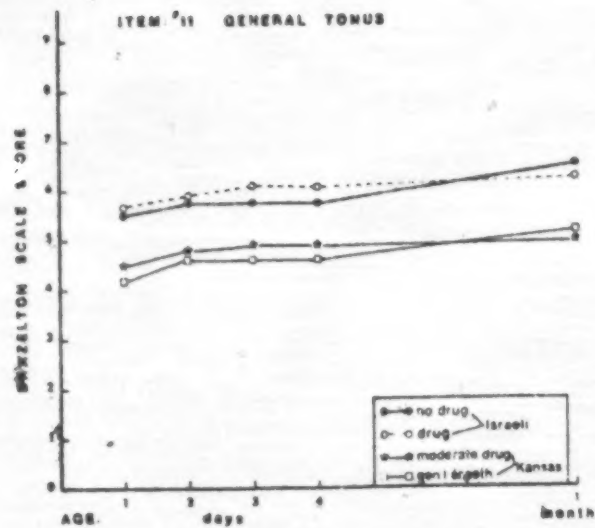
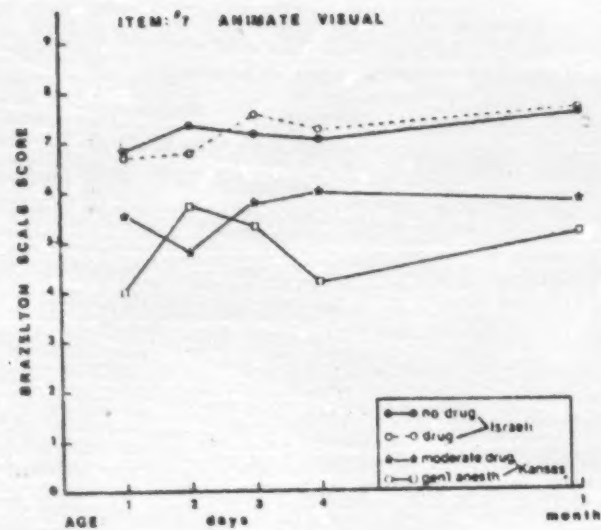
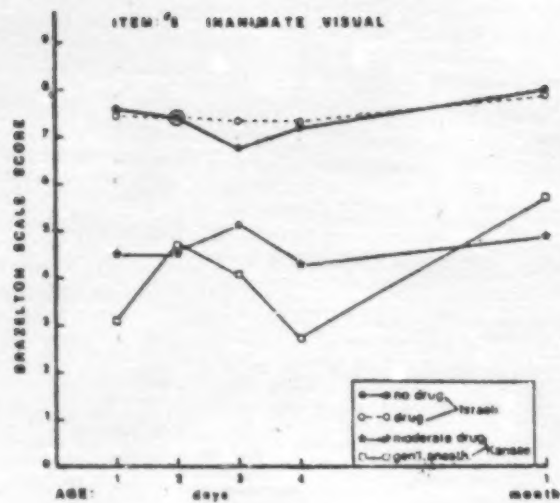


FIGURE 3



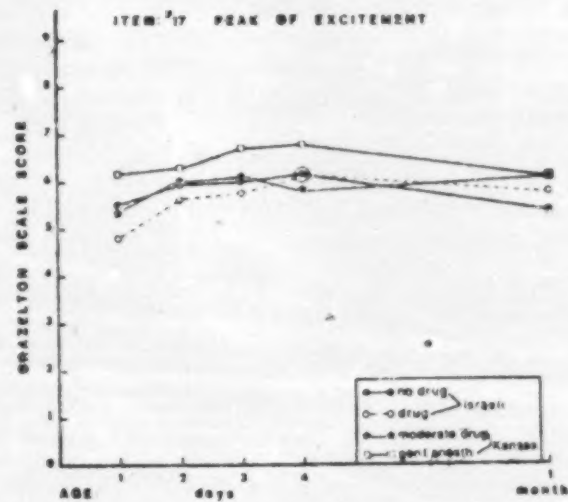
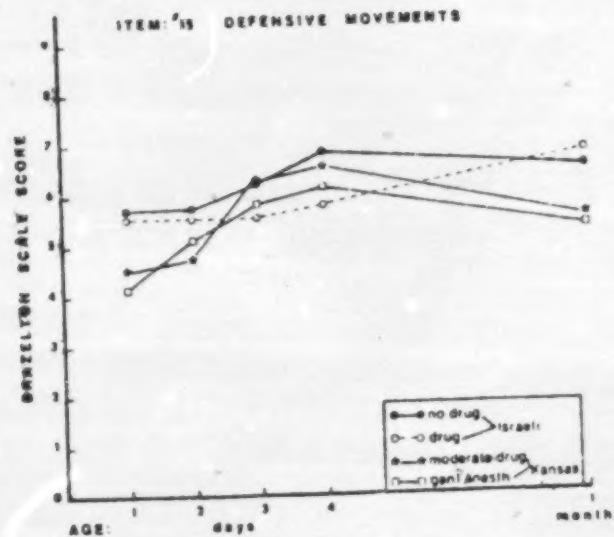
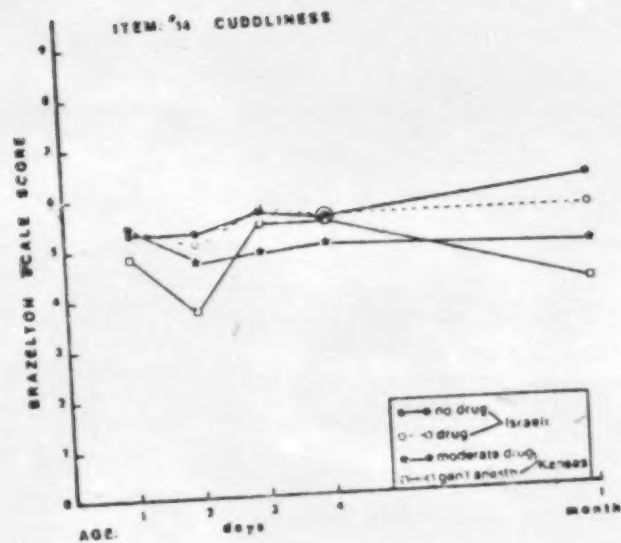
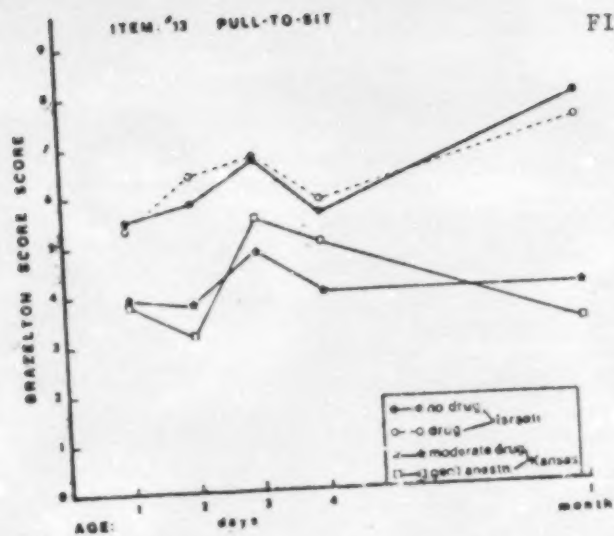


FIGURE 2

